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White Paper:
Ubiquinol

Ubiquinol – potential therapy for heart diseases and considerations in respiratory co-morbidities

WHAT IS UBIQUINOL?

Ubiquinol is the reduced, and more bioavailable, form of Coenzyme Q10 (CoQ10) found in virtually every human cell.[1-4] It is an endogenous lipophilic compound named after it's ubiquitous nature and benzenediol structure. Ubiquinol has a benzenediol ring and hydrophobic polyisoprenoid tail, with two additional hydrogens increasing its polarity and bioavailability compared to ubiquinone, the oxidised form.[3-6] The body must first reduce ubiquinone to Ubiquinol for it to function.[4]

Ubiquinol's role in mitochondrial bioenergetics is well established[2-4], having a key role in electron transport for oxidative phosphorylation in the production of adenosine triphosphate (ATP).[1-4] It is also a potent antioxidant, membrane stabilizer, inhibiting the oxidation of proteins, lipids and DNA.[1-4]

THE MITOCHONDRIA AND ENERGY PRODUCTION

Mitochondria are known as ATP production sites with Ubiquinol key to intracellular energy production, critical for sustaining cellular, and in-turn human life.[10] Subsequently Ubiquinol has an indirect impact on the other functions to which the mitochondria participate such as critical metabolic pathways and integral intracellular signalling networks that regulate diverse cellular functions.[10-12] Mitochondria changes, therefore, have an impact on systemic metabolic regulation, neurogenesis, brain function, inflammation regulation, immunity, aging and life-span.[10,11,13,14]

Mitochondrial dysfunction is recognised as being part of the complex and multifactor pathophysiology for a number of conditions including those of the cardiac[7] and pulmonary system[15], contributing to enhanced reactive oxygen species (ROS) release, and oxidative stress.[15] It is now understood mitochondrial dysfunction has a key role in septic states such as sepsis associated cardiomyopathy, a COVID-19 disease complication, associated with a systemic hyperinflammatory response and myocardial injury.[16] No studies are known to have been conducted in patients with COVID-19.

UBIQUITOUS UBIQUINOL:

- Found in virtually every human cell
- Ubiquinol is more bioavailable than the oxidised form

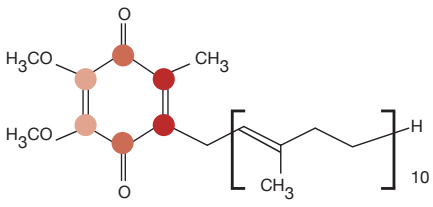
KEY ROLES:

- Mitochondrial oxidative phosphorylation as a cofactor for ATP production.
- Potent antioxidant (by reducing damage in lipid, protein and dicals and their production).
- Cell-membrane stabiliser.

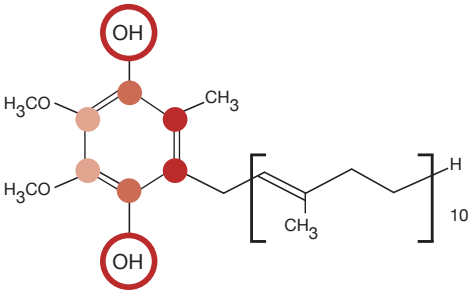
These roles constitute it's broad relevance and potential as an important adjuvant therapy, especially in conditions with mitochondrial dysfunction and oxidative stress, such as some cardiovascular[7] and pulmonary dieases[1,2,8,9], and in age-related conditions.[2,4,6]

Due to its superior bioavailability Ubiquinol is the preferred form of CoQ10 for therapy.[3,4] As such The European Medicine Agency (EMA) has approved ubiquinol for the treatment of primary CoQ10 deficiency.[6]

Ubiquinone (CoQ10)



Ubiquinol (CoQH2)



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CONSIDERATIONS IN CHRONIC HEART FAILURE.[1-3]

Studies in patients with Heart Failure show CoQ10 levels are inversely associated with functional status and severity of Heart Failure symptoms such as fatigue, exercise tolerance and dyspnea.[3,6]

The bioenergetic effects of Ubiquinol are of fundamental importance, especially in cells with high metabolic demand such as cardiac myocytes.[3] Such is the importance that a co-relation is seen with myocardial deficiency and the severity of cardiocirculatory impairment.[3]

Ubiquinol supplementation is an important adjunct therapy to be considered for patients on statins, particularly for those with chronic heart failure and decreased myocardial function.[3]

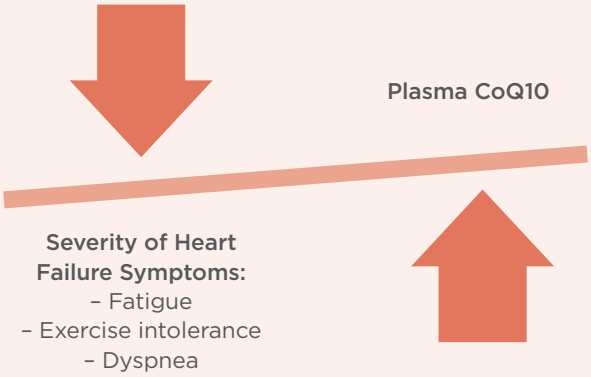
Ubiquinol provides essential energy required for heart muscle function and works as a potent antioxidant. The antioxidant action is two-fold: firstly protecting myocardial cells against potential damage from oxidants, and secondly by reducing oxidant production that could potentially cause damage. Furthermore Ubiquinol supplementation promotes improved cardiovascular relaxation by balancing oxidative and reductive (REDOX) reactions, important in protecting the heart muscle from oxidative or free radical damage.[2,6,18]

Ubiquinol supplementation may also, help alleviate specific Chronic Heart Failure symptoms, shown to be inversely related in severity to low plasma CoQ10 levels,[3,6] such as fatigue and exercise intolerance, [19,22,23] although more specific research for this sub-set is needed.

UBIQUINOL PRODUCTION DECREASES WITH:

- Ageing
- Age-associated diseases
- Inflammation
- Statin use

THE INVERSE RELATIONSHIP OF PLASMA COQ10 LEVELS TO SEVERITY OF HF SYMPTOMS



There is a significant reduction of Ubiquinol synthesis in ageing and diseases associated with ageing,[2,3,6,10,17] accompanied by an increase in oxidative stress due to the imbalance between ROS production and antioxidant defenses.[6,8] Statins impair skeletal muscle and myocardial bioenergetics[3,18] through the inhibition of a key enzyme in the mevalonate pathway, 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) reductase, necessary for cholesterol and CoQ10 production and reduction in mitochondrial complex III activity of the electron transport chain.[3,18]

Supplementation of CoQ10 been demonstrated in a number of studies to alleviate the resulting muscle pain, weakness and fatigue that some patients experience.[2,3,6] Fatigue and exercise endurance has been shown to be improved in healthy subjects supplemented with Ubiquinol.[19-20]

Oral supplementation of Ubiquinol during high-intensity exercise has also been found to reduce the overexpression of pro-inflammatory cytokines and increase in anti-inflammatory cytokines, suggesting a possibly role in modulating exercise-induced inflammation.[21]

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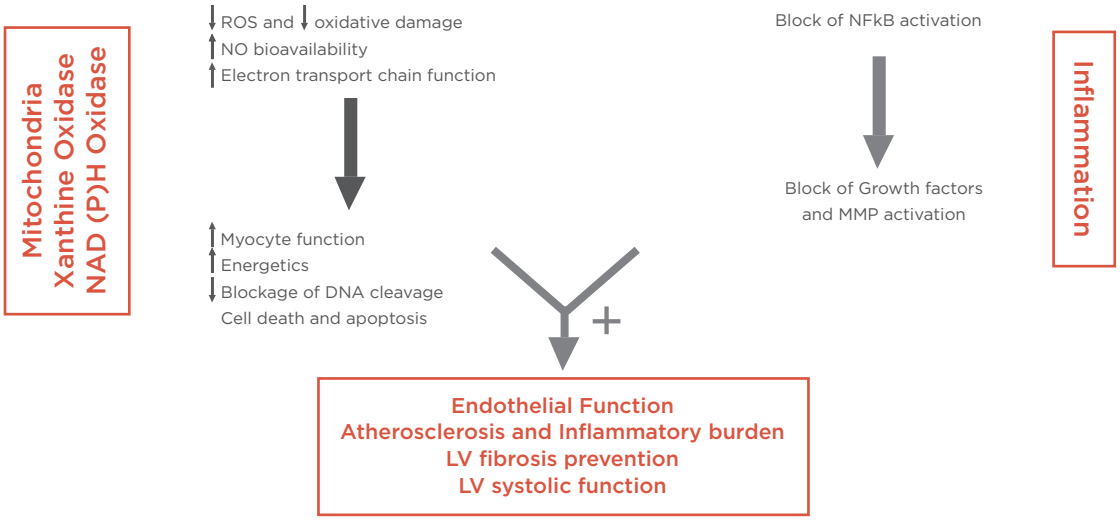
Coenzyme Q10



Clinical benefit on functional status, QoL, and MACE in
HEART FAILURE

Adapted from: Di Lorenzo et al. Clinical Evidence for Q10 Coenzyme Supplementation in Heart Failure: From Energetics to Functional Improvement. J. Clin. Med. 2020, 9, 1266.

COVID-19 CO-MORBIDITY CONSIDERATIONS:

Acute cardiac injury has been reported as important manifestation of COVID-19 infection, and is associated with poor outcomes including increased risk of intensive care admissions and mortality.[16] Cardiac injury tends to occur in older patients, with multiple co-morbidities including hypertension, diabetes, coronary heart disease and heart failure.[16]

PULMONARY CO-MORBIDITY CONSIDERATIONS:

It is well known that acute pulmonary infections have the potential to destabilize cardiac diseases, such as heart failure.[24] Although the role of Ubiquinol supplementation for patients with pulmonary diseases is yet to be established as standard care[25] there is clear involvement of ROS in lung diseases physiopathology.[15] Particular patients, such as those with depressed myocardial function and underlying mitochondrial dysfunction, may potentially benefit from Ubiquinol supplementation. Ubiquinol supplementation, at a daily dose of 300mg, provide improved right and left heart function in patients with Pulmonary Arterial Hypertension, and an improvement in haemoglobin production and red cell maturation.[26]

References supplied on request.

KEY POINTS AND SUMMARY:

- Adequate Ubiquinol is of fundamental importance for all cells, especially those with high metabolic demand such as cardiac myocytes.
- Ubiquinol is essential for healthy cellular and mitochondrial function, energy production, to reduce ROS damage and production and inhibit oxidation.
- A number of factors reduce endogenous Ubiquinol production, including ageing.
- Ubiquinol's benefit in myocardial health is two-fold –
  1. Providing ATP.
  2. Protecting the myocardial from ROS damage and reducing ROS production.
- Acute Cardiac injury is a risk factor for patients with COVID-19 infection and cardiac co-morbidities.
- Ubiquinol supplementation may potentially alleviate some Chronic Heart Failure symptoms, such as fatigue and exercise endurance.
- Pulmonary Arterial Hypertension patients supplemented with Ubiquinol have had some benefit.[26]
- Ubiquinol is more bioavailable than the oxidised form of CoQ10[3,4] and is the preferred supplement form.[3,4]

Ubiquinol

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